## SEQUENCE LISTING

<110> CHUGAI RESEARCH INSTITUTE FOR MOLECULAR MEDICINE, INC.

<120> Tumor suppressor gene

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<150> JP 1999-118806

<151> 1999-04-26

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<170> PatentIn Ver. 2.0

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⟨222⟩ (52).. (1140)

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Ala Ser Gln Ala Glu Val Glu Ser Glu Ala Gly Trp Gly Met Val Thr

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cct gat ctg ctc ttc gcc gag ggg acc gca gcc tac gcg cgc ggg gac 201

Pro Asp Leu Leu Phe Ala Glu Gly Thr Ala Ala Tyr Ala Arg Gly Asp

35 40 45 50

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Trp Pro Gly Val Val Leu Ser Met Glu Arg Ala Leu Arg Ser Arg Ala

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gcc ctc cgc gcc ctt cgc ctg cgc tgc cgc acc cag tgt gcc gcc gac 297

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70 75 80

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Ser	Gly	Ala	Gly	Ala	Leu	Arg	Asp	Leu	Ser	Phe	Phe	Gly	Gly	Leu	Leu	
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Arg	Arg	Ala	Ala	Cys	Leu	Arg	Arg	Cys	Leu	Gly	Pro	Pro	Ala	Ala	His	
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tcg	ctc	agc	gaa	gag	atg	gag	ctg	gag	ttc	cgc	aag	cgg	agc	ccc	tac	489
Ser	Leu	Ser	Glu	Glu	Met	Glu	Leu	Glu	Phe	Arg	Lys	Arg	Ser	Pro	Tyr	
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aac	tac	ctg	cag	gtc	gcc	tac	ttc	aag	atc	aac	aag	ttg	gag	aaa	gct	537
Asn	Tyr	Leu	Gln	Val	Ala	Tyr	Phe	Lys	Ile	Asn	Lys	Leu	Glu	Lys	Ala	
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Val	Ala	Ala	Ala	His	Thr	Phe	Phe	Val	Gly	Asn	Pro	Glu	His	Met	Glu	
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atg cag cag aac cta gac tat tac caa acc atg tct gga gtg aag gag 633 Met Gln Gln Asn Leu Asp Tyr Tyr Gln Thr Met Ser Gly Val Lys Glu

-	42 Äg
	7
	Ī
1	ij
	10 die
1	J
3	à
	rå
	ij
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1	**
	-1

gcc	gac	ttc	aag	gat	ctt	gag	act	caa	ccc	cat	atg	caa	gaa	ttt	cga	681
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His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala Tyr Glu Glu Cys
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cgt gcc ctc tgc gaa ggg ccc tat gac tac gat ggc tac aac tac ctt 825

Arg Ala Leu Cys Glu Gly Pro Tyr Asp Tyr Asp Gly Tyr Asn Tyr Leu

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gag tac aac gct gac ctc ttc cag gcc atc aca gat cat tac atc cag 873

Glu Tyr Asn Ala Asp Leu Phe Gln Ala Ile Thr Asp His Tyr Ile Gln

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gtc ctc aac tgt aag cag aac tgt gtc acg gag ctt gct tcc cac cca 921

Val Leu Asn Cys Lys Gln Asn Cys Val Thr Glu Leu Ala Ser His Pro

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agt cga gag aag ccc ttt gaa gac ttc ctc cca tcg cat tat aat tat 969

Ser Arg Glu Lys Pro Phe Glu Asp Phe Leu Pro Ser His Tyr Asn Tyr

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Gly Asp Trp Pro Gly Val Val Leu Ser Met Glu Arg Ala Leu Arg Ser
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Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Gln Cys Ala 65 70 75 80

Ala Asp Phe Pro Trp Glu Leu Asp Pro Asp Trp Ser Pro Ser Pro Ala

85 90 95

Gln Ala Ser Gly Ala Gly Ala Leu Arg Asp Leu Ser Phe Phe Gly Gly
100 105 110

Leu Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys Leu Gly Pro Pro Ala
115 120 -125

Ala His Ser Leu Ser Glu Glu Met Glu Leu Glu Phe Arg Lys Arg Ser

130 135 140

Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys Ile Asn Lys Leu Glu
145 150 155 160

Lys Ala Val Ala Ala Ala His Thr Phe Phe Val Gly Asn Pro Glu His

165 170 175

Met Glu Met Gln Gln Asn Leu Asp Tyr Tyr Gln Thr Met Ser Gly Val
180 185 190

Lys Glu Ala Asp Phe Lys Asp Leu Glu Thr Gln Pro His Met Gln Glu
195 200 205

Phe Arg Leu Gly Val Arg Leu Tyr Ser Glu Glu Gln Pro Gln Glu Ala 210 215 220

Val Pro His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala Tyr Glu 225 230 235 240

Glu Cys Arg Ala Leu Cys Glu Gly Pro Tyr Asp Tyr Asp Gly Tyr Asn 245 250 255 Tyr Leu Glu Tyr Asn Ala Asp Leu Phe Gln Ala Ile Thr Asp His Tyr

260 265 270

Ile Gln Val Leu Asn Cys Lys Gln Asn Cys Val Thr Glu Leu Ala Ser 275 280 285

His Pro Ser Arg Glu Lys Pro Phe Glu Asp Phe Leu Pro Ser His Tyr
290 295 300

Asn Tyr Leu Gln Phe Ala Tyr Tyr Asn Ile Gly Asn Tyr Thr Gln Ala 305 310 315 320

Gly Glu Cys Ala Lys Thr Tyr Leu Leu Phe Phe Pro Asn Asp Glu Val
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Val Arg Ala Leu Lys Leu Leu Thr Thr Leu Leu Ala Val Val Ala Ala

5 10 15

gcc tcc caa gcc gag gtc gag tcc gag gca gga tgg ggc atg gtg acg 153

Ala Ser Gln Ala Glu Val Glu Ser Glu Ala Gly Trp Gly Met Val Thr

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cct gat ctg ctc ttc gcc gag ggg acc gca gcc tac gcg cgc ggg gac 201
Pro Asp Leu Leu Phe Ala Glu Gly Thr Ala Ala Tyr Ala Arg Gly Asp
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Trp Pro Gly Val Val Leu Ser Met Glu Arg Ala Leu Arg Ser Arg Ala

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	Ser	Gly	Ala	G1y	Ala	Leu	Arg	Asp	Leu	Ser	Phe	Phe	Gly	Gly	Leu	Leu	
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	Arg	Arg	Ala	Ala	Cys	Leu	Arg	Arg	Cys	Leu	G1y	Pro	Pro	Ala	Ala	His	
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1	Ser	Leu	Ser	Glu	Glu	Met	Glu	Leu	Glu	Phe	Arg	Lys	Arg	Ser	Pro	Tyr	
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č	aac	tac	ctg	cag	gtc	gcc	tac	ttc	aag	atc	aac	aag	ttg	gag	aaa	gct	537

gtt gct gca gca cac acc ttc ttc gtg ggc aat cct gag cac atg gaa  $\phantom{0}585$ 

155

160

Asn Tyr Leu Gln Val Ala Tyr Phe Lys Ile Asn Lys Leu Glu Lys Ala

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Val	$Ala_{.}$	Ala	Ala	His	Thr	Phe	Phe	Val	Gly	Asn	Pro	Glu	His	Met	Glu
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ctg gga gtg cga ctc tac tca gag gaa cag cca cag gaa gct gtg ccc 729

Leu Gly Val Arg Leu Tyr Ser Glu Glu Gln Pro Gln Glu Ala Val Pro
215 220 225

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His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala Tyr Glu Glu Cys

230 235 240

cgt gcc ctc tgc gaa ggg ccc tat gac tac gat ggc tac aac tac ctt 825

Arg Ala Leu Cys Glu Gly Pro Tyr Asp Tyr Asp Gly Tyr Asn Tyr Leu

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Glu Tyr Asn Ala Asp Leu Phe Gln Ala Ile Thr Asp His Tyr Ile Gln
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Ser	Arg	Glu	Lys	Pro	Phe	Glu	Asp	Phe	Leu	Pro	Ser	His	Tyr	Asn	Tyr	
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.+	~~~	+++	~~~	+	+ - +		.++		+	4_4					222	1017
	cag															1017
Leu	Gln	Phe	Ala	Tyr	Tyr	Asn	lle	Gly	Asn	Tyr	Thr	Gln	Ala	Gly	Glu	
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Cys	Ala	Lys	Thr	Tyr	Leu	Leu	Phe	Phe	Pro	Asn	Asp	Glu	Val	Met	Asn	
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caa	aat	ttg	gcc	tat	tat	gca	gct	atg	ctt	gga	gaa	gaa	cac	acc	aga	1113
Gln	Asn	Leu	Ala	Tyr	Tyr	Ala	Ala	Met	Leu	Gly	Glu	Glu	His	Thr	Arg	
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+	a+-	~~~	000	a=+	<b>~</b> .~	0.54	<b></b>		<b></b> -	<b>.</b>					. 4 .	1101
	atc															1161
	Ile	Gly	Pro	Arg		Ser	Ala	Lys	Glu	Tyr	Arg	Gln	Arg	Ser	Leu	
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Leu Glu Lys Glu Leu Leu Phe Phe Ala Tyr Asp Val Phe Gly Ile Pro 375 380 - 385

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Phe Val Asp Pro Asp Ser Trp Thr Pro Glu Glu Val Ile Pro Lys Arg
390 395 400

ttg caa gag aaa cag aag tca gaa cgg gaa aca gcc gta cgc atc tcc 1305 Leu Gln Glu Lys Gln Lys Ser Glu Arg Glu Thr Ala Val Arg Ile Ser 405 410 415

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aag acc aag gag tca ctg gat gtg agc aga ctg acc cgg gaa ggt ggc 1401 Lys Thr Lys Glu Ser Leu Asp Val Ser Arg Leu Thr Arg Glu Gly Gly 435 440 445 450

ccc ctg ctg tat gaa ggc atc agt ctc acc atg aac tcc aaa ctc ctg 1449

Pro Leu Leu Tyr Glu Gly Ile Ser Leu Thr Met Asn Ser Lys Leu Leu

455

460

465

aat ggt tac cag cgg gtg gtg atg gac ggc gta atc tct gac cac gag 1497 Asn Gly Tyr Gln Arg Val Val Met Asp Gly Val Ile Ser Asp His Glu 470 475 480 tgt cag gag ctg cag aga ctg acc aat gtg gca gca acc tca gga gat 1545 Cys Gln Glu Leu Gln Arg Leu Thr Asn Val Ala Ala Thr Ser Gly Asp 485 490 495

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Gly Tyr Arg Gly Gln Thr Ser Pro His Thr Pro Asn Glu Lys Phe Tyr

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Pro Leu Gln Ser Ala His Leu Tyr Tyr Asn Val Thr Glu Lys Val Arg
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cgc atc atg gag tcc tac ttc cgc ctg gat acg ccc ctc tac ttt tcc 1737

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550 555 560

tac tct cat ctg gtg tgc cgc act gcc atc gaa gag gtc cag gca gag 1785

Tyr Ser His Leu Val Cys Arg Thr Ala Ile Glu Glu Val Gln Ala Glu

565 570 575

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Arg Lys Asp Asp Ser His Pro Val His Val Asp Asn Cys Ile Leu Asn 580 585 590

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Ala Glu Thr Leu Val Cys Val Lys Glu Pro Pro Ala Tyr Thr Phe Arg

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His Gly Val Lys Ala Val Thr Arg Gly Gln Arg Cys Ala Ile Ala Leu

660 665 670

tgg ttc acc ctg gac cct cga cac agc gag cgg gac agg gtg cag gca 2121

Trp Phe Thr Leu Asp Pro Arg His Ser Glu Arg Asp Arg Val Gln Ala

675 680 685 690

gat gac ctg gtg aag atg ctc ttc agc cca gaa gag atg gac ctc tcc 2169

Asp Asp Leu Val Lys Met Leu Phe Ser Pro Glu Glu Met Asp Leu Ser

695 700 705

cag gag cag ccc ctg gat gcc cag cag ggc ccc ccc gaa cct gca caa 2217

Gln Glu Gln Pro Leu Asp Ala Gln Gln Gly Pro Pro Glu Pro Ala Gln

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gag tet etc tea gge agt gaa teg aag eec aag gat gag eta 2259

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Gln Ala Ser Gly Ala Gly Ala Leu Arg Asp Leu Ser Phe Phe Gly Gly

Leu Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys Leu Gly Pro Pro Ala 115 120 125

Ala His Ser Leu Ser Glu Glu Met Glu Leu Glu Phe Arg Lys Arg Ser

130 135 140

Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys Ile Asn Lys Leu Glu 145 150 155 160

Lys Ala Val Ala Ala Ala His Thr Phe Phe Val Gly Asn Pro Glu His

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Met Glu Met Gln Gln Asn Leu Asp Tyr Tyr Gln Thr Met Ser Gly Val
180 185 190

Lys Glu Ala Asp Phe Lys Asp Leu Glu Thr Gln Pro His Met Gln Glu
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Phe Arg Leu Gly Val Arg Leu Tyr Ser Glu Glu Gln Pro Gln Glu Ala 210 215 220

Val Pro His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala Tyr Glu 225 230 235 240

Glu Cys Arg Ala Leu Cys Glu Gly Pro Tyr Asp Tyr Asp Gly Tyr Asn

House South Street Street He

245

Tyr Leu Glu Tyr Asn Ala Asp Leu Phe Gln Ala Ile Thr Asp His Tyr

260 265 270

Ile Gln Val Leu Asn Cys Lys Gln Asn Cys Val Thr Glu Leu Ala Ser 275 280 285

His Pro Ser Arg Glu Lys Pro Phe Glu Asp Phe Leu Pro Ser His Tyr
290 295 300

Asn Tyr Leu Gln Phe Ala Tyr Tyr Asn Ile Gly Asn Tyr Thr Gln Ala 305 310 315 320

Gly Glu Cys Ala Lys Thr Tyr Leu Leu Phe Phe Pro Asn Asp Glu Val

325
330
335

Met Asn Gln Asn Leu Ala Tyr Tyr Ala Ala Met Leu Gly Glu Glu His

340 345 350

Thr Arg Ser Ile Gly Pro Arg Glu Ser Ala Lys Glu Tyr Arg Gln Arg 355 360 365

Ser Leu Leu Glu Lys Glu Leu Leu Phe Phe Ala Tyr Asp Val Phe Gly 370 375 380

Ile Pro Phe Val Asp Pro Asp Ser Trp Thr Pro Glu Glu Val Ile Pro 385 390 395 400

Lys Arg Leu Gln Glu Lys Gln Lys Ser Glu Arg Glu Thr Ala Val Arg
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Ile Ser Gln Glu Ile Gly Asn Leu Met Lys Glu Ile Glu Thr Leu Val
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Glu Glu Lys Thr Lys Glu Ser Leu Asp Val Ser Arg Leu Thr Arg Glu
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Gly Gly Pro Leu Leu Tyr Glu Gly Ile Ser Leu Thr Met Asn Ser Lys
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His Glu Cys Gln Glu Leu Gln Arg Leu Thr Asn Val Ala Ala Thr Ser 485 490 495

Gly Asp Gly Tyr Arg Gly Gln Thr Ser Pro His Thr Pro Asn Glu Lys
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Lys Val Pro Leu Gln Ser Ala His Leu Tyr Tyr Asn Val Thr Glu Lys
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Val Arg Arg Ile Met Glu Ser Tyr Phe Arg Leu Asp Thr Pro Leu Tyr 545 550 555 560

Phe Ser Tyr Ser His Leu Val Cys Arg Thr Ala Ile Glu Glu Val Gln
565 570 575

Ala Glu Arg Lys Asp Asp Ser His Pro Val His Val Asp Asn Cys Ile
580 585 590

Leu Asn Ala Glu Thr Leu Val Cys Val Lys Glu Pro Pro Ala Tyr Thr
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Phe Arg Asp Tyr Ser Ala Ile Leu Tyr Leu Asn Gly Asp Phe Asp Gly 610 615 620

Gly Asn Phe Tyr Phe Thr Glu Leu Asp Ala Lys Thr Val Thr Ala Glu
625 630 635 640

Val Gln Pro Gln Cys Gly Arg Ala Val Gly Phe Ser Ser Gly Thr Glu
645 650 655

Asn Pro His Gly Val Lys Ala Val Thr Arg Gly Gln Arg Cys Ala Ile

The fact of the fact that the most the total and the fact that the

Ala Leu Trp Phe Thr Leu Asp Pro Arg His Ser Glu Arg Asp Arg Val 675 680 685

Gln Ala Asp Asp Leu Val Lys Met Leu Phe Ser Pro Glu Glu Met Asp 690 695 700

Leu Ser Gln Glu Gln Pro Leu Asp Ala Gln Gln Gly Pro Pro Glu Pro 705 710 715 720

Ala Gln Glu Ser Leu Ser Gly Ser Glu Ser Lys Pro Lys Asp Glu Leu
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G1y	Arg	Arg	Arg	Arg	Arg	Leu	Thr	Gly	Cys	Gly	Glu	Ser	Glu	Pro	G1y	
	15					20					25					

tgg gac gtg gca gcc cct gac ctg ctt tac gca gag ggg acc gcg gcc 146
Trp Asp Val Ala Ala Pro Asp Leu Leu Tyr Ala Glu Gly Thr Ala Ala
30 35 40 45

tac tcg cgc agg gac tgg ccc ggg gtg gtc ctg aac atg gag cgg gct 194

Tyr Ser Arg Arg Asp Trp Pro Gly Val Val Leu Asn Met Glu Arg Ala

50 55 60

ctg cgc tcg cgg gcc ctg cgt gcc ctc cgc ctg cgc tgc cgc aca 242

Leu Arg Ser Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr

65 70 75

cgc tgt gcc acc gaa ctg ccg tgg gca ccg gac ctg gat ctc ggt ccg 290

Arg Cys Ala Thr Glu Leu Pro Trp Ala Pro Asp Leu Asp Leu Gly Pro

80 85 90

gac ccc agc ctg agc cag gac ccg ggc gcc gcc gcc ctg cac gac ctg 338

Asp Pro Ser Leu Ser Gln Asp Pro Gly Ala Ala Ala Leu His Asp Leu

95 100 105

cgc	ttc	ttc	gga	gcc	gtg	ctg	cgc	cgt	gcc	gcc	tgc-	cta	cgc	cgc	tgc	380
Arg	Phe	Phe	Gly	Ala	Val	Leu	Arg	Arg	Ala	Ala	Cys	Leu	Arg	Arg	Cys	
110					115					120					125	
ctc	ggg	ccg	ccc	tct	gcc	cac	ttg	ctg	agt	gaa	gaa	ctg	gac	ctg	gag	434
Leu	G1y	Pro	Pro	Ser	Ala	His	Leu	Leu	Ser	Glu	Glu	Leu	Asp	Leu	Glu	
				130					135					140		
ttc	990	990	റത്ത	age	cca	tac	aac	tac	cta	്രദ	atc	gee	tat	ttc	aao	482
																102
rne	ASII	Lys		ser	FIO	1 у Г	ASII	Tyr	Leu	GIU	Val	Ala		rne	Lys	
			145					150					155			
ata	aac	aag	ctg	gag	aaa	gct	gtg	gct	gcg	gca	cac	acc	ttc	ttt	gtg	530
Ile	Asn	Lys	Leu	Glu	Lys	Ala	Va1	Ala	Ala	Ala	His	Thr	Phe	Phe	Val	
		160					165					170				
ggc	aat	cct	gag	cac	atg	gag	atg	cgg	cag	aac	ctc	gac	tat	tac	caa	578
Gly	Asn	Pro	Glu	His	Met	Glu	Met	Arg	Gln	Asn	Leu	Asp	Tyr	Tyr	Gln	
	175					180					185					
acc	atg	tct	ggg	gtg	aag	gag	gca	gac	ttc	agg	gat	ctc	gag	gcc	aag	626
								Asp								
190			,		195			P		200	h				205	
100		,			100					200					200	

ccc cat atg cat gag ttt cgg ctg ggg gta cga ctc tac tca gag gag 674

Pro	His	Met	His	Glu	Phe	Arg	Leu	Gly	Val	Arg	Leu	Tyr	Ser	Glu	Glu	
				210					215		-			220		
aag	cca	cag	gaa	gct	gtg	ccc	cac	ctg	gag	gcg	gca	ctg	caa	gag	tac	722
Lys	Pro	Gln	Glu	Ala	Va1	Pro	His	Leu	Glu	Ala	Ala	Leu	Gln	Glu	Tyr	
			225					230					235			
														,		
ttt	gtg	gcc	gat	gag	gag	tgc	cgt	gcc	ctc	tgc	gaa	ggg	ccc	tat	gac	770
Phe	Val	Ala	Asp	Glu	Glu	Cys	Arg	Ala	Leu	Cys	Glu	Gly	Pro	Tyr	Asp	
		240					245					250				
tac	gac	ggc	tac	aac	tac	cta	gac	tac	agc	gct	gac	ctc	ttc	cag	gcc	818
Tyr	Asp	Gly	Tyr	Asn	Tyr	Leu	Asp	Tyr	Ser	Ala	Asp	Leu	Phe	Gln	Ala	
	255					260					265					
atc	aca	gat	cat	tac	gtc	cag	gtc	ctc	aac	tgt	aag	cag	aac	tgt	gtc	866
Ile	Thr	Asp	His	Tyr	Val	Gln	Val	Leu	Asn	Cys	Lys	Gln	Asn	Cys	Val	
270					275					280					285	
acg	gag	ctg	gct	tcc	cac	cca	agt	agg	gaa	aag	ссс	ttt	gaa	gac	ttc	914
Thr	Glu	Leu	Ala	Ser	His	Pro	Ser	Arg	Glu	Lys	Pro	Phe	Glu	Asp	Phe	
				290					295					300		
ctc	cct	tca	cac	tat	aat	tac	cta	cag	ttt	gcc	tac	tac	aac	att	ggg	962
Leu																

aac tat aca caa gct att gaa tgt gcc aag acc tac ctc ctc ttc ttt 1010
Asn Tyr Thr Gln Ala Ile Glu Cys Ala Lys Thr Tyr Leu Leu Phe Phe
320 325 330

ccc aat gat gag gtg atg cac cag aat ctg gct tat tac aca gcc atg 1058

Pro Asn Asp Glu Val Met His Gln Asn Leu Ala Tyr Tyr Thr Ala Met

335 340 345

ctt gga gaa gaa gag gcc agc tcc atc agc ccc agg gag aat gcc gag 1106 Leu Gly Glu Glu Glu Ala Ser Ser Ile Ser Pro Arg Glu Asn Ala Glu 350 355 360 365

gaa tac cga cgt cca aac ctg ttg gag aaa gaa ctg ctt ttc ttc gct 1154

Glu Tyr Arg Arg Pro Asn Leu Leu Glu Lys Glu Leu Leu Phe Phe Ala

370 375 380

tat gac att ttt gga att ccc ttt gtg gat ccc gat tca tgg act cca 1202

Tyr Asp Ile Phe Gly Ile Pro Phe Val Asp Pro Asp Ser Trp Thr Pro

385 390 395

gaa gaa gtg att ccc aag aga ttg caa gag aaa cag aag tct gaa cgg 1250 Glu Glu Val Ile Pro Lys Arg Leu Gln Glu Lys Gln Lys Ser Glu Arg 400 405 410

gaa aca gcc gta cgc atc tcc cag gag att ggg aac ctt atg aag gaa 1298

Glu Thr Ala Val Arg Ile Ser Gln Glu Ile Gly Asn Leu Met Lys Glu
415 420 425

atc gag acc ctt gtg gaa gag aag acc aag gag tct ctg gat gtg agc 1346

Ile Glu Thr Leu Val Glu Glu Lys Thr Lys Glu Ser Leu Asp Val Ser

430 435 440 445

aga ctg acc cgg gaa ggt ggt ccc ctg ctg tat gaa ggc atc agt ctc 1394

Arg Leu Thr Arg Glu Gly Gly Pro Leu Leu Tyr Glu Gly Ile Ser Leu

450

455

460

acc atg aac tcc aaa gtc ttg aat ggc tcc cag cgg gtg gtg atg gat 1442

Thr Met Asn Ser Lys Val Leu Asn Gly Ser Gln Arg Val Val Met Asp
465 470 475

ggt gtg atc tct gat gat gag tgc cag gag ctg cag aga ctg acc aat 1490 Gly Val Ile Ser Asp Asp Glu Cys Gln Glu Leu Gln Arg Leu Thr Asn 480 485 490

gcg gca gca act tcg gga gat ggc tac cga ggt cag acc tcc cca cac 1538

Ala Ala Ala Thr Ser Gly Asp Gly Tyr Arg Gly Gln Thr Ser Pro His

495 500 505

acc cca aat gaa aag ttc tat ggt gtt act gtc ctc aaa gct ctc aag 1586

Thr Pro Asn Glu Lys Phe Tyr Gly Val Thr Val Leu Lys Ala Leu Lys

510 525

ctc ggg cag gaa gga aaa gtt cct ctg cag agt gcc cgc atg tac tac 1634 Leu Gly Gln Glu Gly Lys Val Pro Leu Gln Ser Ala Arg Met Tyr Tyr 530 535 540 aac gtg aca gag aag gtg cgg cgc gtc atg gag tcc tac ttc cgc ctg 1682 Asn Val Thr Glu Lys Val Arg Arg Val Met Glu Ser Tyr Phe Arg Leu 545 550 555 gac acg ccc ctc tat ttc tct tat tcc cac ttc gtg tgc cgc act gca 1730 Asp Thr Pro Leu Tyr Phe Ser Tyr Ser His Phe Val Cys Arg Thr Ala 560 565 570 ata gaa gag tca cag gct gag agg aag gac agt agc cac ccc gtc cac 1778 Ile Glu Glu Ser Gln Ala Glu Arg Lys Asp Ser Ser His Pro Val His 575 580 585 gtg gat aac tgc atc ctg aat gcc gaa gcc ttc atg tgt atc aag gag 1826 Val Asp Asn Cys Ile Leu Asn Ala Glu Ala Phe Met Cys Ile Lys Glu 590 595 600 605

ccc cca gca tac acg ttc cgg gaa tac agc gcc atc ctt tac ctc aat 1874
Pro Pro Ala Tyr Thr Phe Arg Glu Tyr Ser Ala Ile Leu Tyr Leu Asn
610 615 620

ggc gac ttc gat gga gga aac ttt tac ttc aca gaa cta gat gcc aag 1922

Gly	Asp	Phe	Asp	Gly	Gly	Asn	Phe	Tyr	Phe	Thr	Glu	Leu	Asp	Ala	Lys
			625					630			-		635		

act gtg acg gca gag gtg cag ccc cag tgt gga agg gct gtg gga ttc 1970

Thr Val Thr Ala Glu Val Gln Pro Gln Cys Gly Arg Ala Val Gly Phe
640 645 650

tct tct ggc act gag aac cca cat gga gtg aag gct gtc acc agg ggg 2018

Ser Ser Gly Thr Glu Asn Pro His Gly Val Lys Ala Val Thr Arg Gly

655 660 665

cag cgc tgc gcc atc gcc ctg tgg ttc acg ctg gat cct cgg cac agt 2066

Gln Arg Cys Ala Ile Ala Leu Trp Phe Thr Leu Asp Pro Arg His Ser

670 680 685

gag aga gac agg gtg cag gca gat gac ctg gtg aag atg ctg ttc agc 2114

Glu Arg Asp Arg Val Gln Ala Asp Asp Leu Val Lys Met Leu Phe Ser

690 695 700

cca gaa gag gtg gac ctc ccc cag gaa cag ccc ctg cct gac cag cag 2162
Pro Glu Glu Val Asp Leu Pro Gln Glu Gln Pro Leu Pro Asp Gln Gln
705 710 715

ggt tcg cca gag cct gga gaa gag ttt ctg cat ggt gct act gtt ctt 2210

Gly Ser Pro Glu Pro Gly Glu Glu Phe Leu His Gly Ala Thr Val Leu

720 725 730

gga gtg ggc ata gca gga cac act ctt ctc tgg gct tgg ctg
Gly Val Gly Ile Ala Gly His Thr Leu Leu Trp Ala Trp Leu
735 740 745

taggeteaga atgeaggeee agaaceaeee tggggeetat gtaggeaget geegteagea 2312

gcgtgatata tttaagtgtc tgtaaagaca accaaagaat aaatgatttg tgtttttaaa 2372

aagnaaaaaa aaaaaaaaat taaaaatttg cgcggccgca agaa

2416

2252

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Ala Ala Pro Asp Leu Leu Tyr Ala Glu Gly Thr Ala Ala Tyr Ser Arg

35 40 45

Arg Asp Trp Pro Gly Val Val Leu Asn Met Glu Arg Ala Leu Arg Ser 50 55 60

Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Arg Cys Ala
65 70 75 80

Thr Glu Leu Pro Trp Ala Pro Asp Leu Asp Leu Gly Pro Asp Pro Ser

85 90 95

Leu Ser Gln Asp Pro Gly Ala Ala Ala Leu His Asp Leu Arg Phe Phe
100 105 110

Gly Ala Val Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys Leu Gly Pro 115 120 125

Pro Ser Ala His Leu Leu Ser Glu Glu Leu Asp Leu Glu Phe Asn Lys
130 135 140

Arg Ser Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys Ile Asn Lys
145 150 155 160

Leu Glu Lys Ala Val Ala Ala Ala His Thr Phe Phe Val Gly Asn Pro 165 170 175

Glu His Met Glu Met Arg Gln Asn Leu Asp Tyr Tyr Gln Thr Met Ser

180 185 190

Gly Val Lys Glu Ala Asp Phe Arg Asp Leu Glu Ala Lys Pro His Met
195 200 205

His Glu Phe Arg Leu Gly Val Arg Leu Tyr Ser Glu Glu Lys Pro Gln
210 215 220

Glu Ala Val Pro His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala 225 230 235 240

Asp Glu Glu Cys Arg Ala Leu Cys Glu Gly Pro Tyr Asp Tyr Asp Gly
245 250 255

Tyr Asn Tyr Leu Asp Tyr Ser Ala Asp Leu Phe Gln Ala Ile Thr Asp
260 265 270

His Tyr Val Gln Val Leu Asn Cys Lys Gln Asn Cys Val Thr Glu Leu 275 280 285

Ala Ser His Pro Ser Arg Glu Lys Pro Phe Glu Asp Phe Leu Pro Ser 290 295 300

His Tyr Asn Tyr Leu Gln Phe Ala Tyr Tyr Asn Ile Gly Asn Tyr Thr 305 310 315 320 Gln Ala Ile Glu Cys Ala Lys Thr Tyr Leu Leu Phe Phe Pro Asn Asp 325 330 - 335

Glu Val Met His Gln Asn Leu Ala Tyr Tyr Thr Ala Met Leu Gly Glu
340 345 350

Glu Glu Ala Ser Ser Ile Ser Pro Arg Glu Asn Ala Glu Glu Tyr Arg 355 360 365

Arg Pro Asn Leu Leu Glu Lys Glu Leu Leu Phe Phe Ala Tyr Asp Ile 370 375 380

Phe Gly Ile Pro Phe Val Asp Pro Asp Ser Trp Thr Pro Glu Glu Val 385 390 395 400

Ile Pro Lys Arg Leu Gln Glu Lys Gln Lys Ser Glu Arg Glu Thr Ala
405 410 415

Val Arg Ile Ser Gln Glu Ile Gly Asn Leu Met Lys Glu Ile Glu Thr
420 425 430

Leu Val Glu Glu Lys Thr Lys Glu Ser Leu Asp Val Ser Arg Leu Thr
435
440
445

Arg Glu Gly Gly Pro Leu Leu Tyr Glu Gly Ile Ser Leu Thr Met Asn 450 455 460 Ser Lys Val Leu Asn Gly Ser Gln Arg Val Val Met Asp Gly Val Ile 465 470 475 480

Ser Asp Asp Glu Cys Gln Glu Leu Gln Arg Leu Thr Asn Ala Ala Ala 485 490 495

Thr Ser Gly Asp Gly Tyr Arg Gly Gln Thr Ser Pro His Thr Pro Asn 500 505 510

Glu Lys Phe Tyr Gly Val Thr Val Leu Lys Ala Leu Lys Leu Gly Gln
515 520 525

Glu Gly Lys Val Pro Leu Gln Ser Ala Arg Met Tyr Tyr Asn Val Thr
530 535 540

Glu Lys Val Arg Arg Val Met Glu Ser Tyr Phe Arg Leu Asp Thr Pro 545 550 555 560

Leu Tyr Phe Ser Tyr Ser His Phe Val Cys Arg Thr Ala Ile Glu Glu
565 570 575

Ser Gln Ala Glu Arg Lys Asp Ser Ser His Pro Val His Val Asp Asn 580 585 590

Cys Ile Leu Asn Ala Glu Ala Phe Met Cys Ile Lys Glu Pro Pro Ala

Tyr Thr Phe Arg Glu Tyr Ser Ala Ile Leu Tyr Leu Asn Gly Asp Phe 

Asp Gly Gly Asn Phe Tyr Phe Thr Glu Leu Asp Ala Lys Thr Val Thr 

Ala Glu Val Gln Pro Gln Cys Gly Arg Ala Val Gly Phe Ser Ser Gly 

Thr Glu Asn Pro His Gly Val Lys Ala Val Thr Arg Gly Gln Arg Cys 

Ala Ile Ala Leu Trp Phe Thr Leu Asp Pro Arg His Ser Glu Arg Asp 

Arg Val Gln Ala Asp Asp Leu Val Lys Met Leu Phe Ser Pro Glu Glu 

Val Asp Leu Pro Gln Glu Gln Pro Leu Pro Asp Gln Gln Gly Ser Pro 

Glu Pro Gly Glu Glu Phe Leu His Gly Ala Thr Val Leu Gly Val Gly 

Ile Ala Gly His Thr Leu Leu Trp Ala Trp Leu
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<400> 7

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Met Ala Val Thr Lys Gly Gly Cys Trp His Asp Ala Ser

1 5 10

ggt cgc cgc cgc cgc ctt acg ggt tgc ggc gag tct gag ccg gga 98

Gly Arg Arg Arg Arg Leu Thr Gly Cys Gly Glu Ser Glu Pro Gly

20 25

tgg gac gtg gca gcc cct gac ctg ctt tac gca gag ggg acc gcg gcc 146
Trp Asp Val Ala Ala Pro Asp Leu Leu Tyr Ala Glu Gly Thr Ala Ala
30 35 40 45

tac tcg cgc agg gac tgg ccc ggg gtg gtc ctg aac atg gag cgg gct Tyr Ser Arg Arg Asp Trp Pro Gly Val Val Leu Asn Met Glu Arg Ala ctg cgc tcg cgg gcc ctg cgt gcc ctc cgc ctg cgc tgc cgc aca Leu Arg Ser Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr ege tgt gee ace gaa etg eeg tgg gea eeg gae etg gat ete ggt eeg Arg Cys Ala Thr Glu Leu Pro Trp Ala Pro Asp Leu Asp Leu Gly Pro gac ccc agc ctg agc cag gac ccg ggc gcc gcc ctg cac gac ctg Asp Pro Ser Leu Ser Gln Asp Pro Gly Ala Ala Ala Leu His Asp Leu cgc ttc ttc gga gcc gtg ctg cgc cgt gcc gcc tgc cta cgc cgc tgc Arg Phe Phe Gly Ala Val Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys ctc ggg ccg ccc tct gcc cac ttg ctg agt gaa gaa ctg gac ctg gag Leu Gly Pro Pro Ser Ala His Leu Leu Ser Glu Glu Leu Asp Leu Glu 

ttc aac aag cgg agc ccg tac aac tac ctg cag gtc gcc tat ttc aag
Phe Asn Lys Arg Ser Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys

and given groups if it present given and groups and given and given in the state of the state of

ata	aac	aag	ctg	gag	aaa	gct	gtg	gct	gcg	gca	cac	acc	ttc	ttt	gtg	530
Ile	Asn	Lys	Leu	Glu	Lys	Ala	Val	Ala	Ala	Ala	His	Thr	Phe	Phe	Val	
		160					165					170				

ggc aat cct gag cac atg gag atg cgg cag aac ctc gac tat tac caa Gly Asn Pro Glu His Met Glu Met Arg Gln Asn Leu Asp Tyr Tyr Gln 

acc atg tct ggg gtg aag gag gca gac ttc agg gat ctc gag gcc aag Thr Met Ser Gly Val Lys Glu Ala Asp Phe Arg Asp Leu Glu Ala Lys 

ccc cat atg cat gag ttt cgg ctg ggg gta cga ctc tac tca gag gag Pro His Met His Glu Phe Arg Leu Gly Val Arg Leu Tyr Ser Glu Glu 

aag cca cag gaa gct gtg ccc cac ctg gag gcg gca ctg caa gag tac Lys Pro Gln Glu Ala Val Pro His Leu Glu Ala Ala Leu Gln Glu Tyr 

ttt gtg gcc gat gag gag tgc cgt gcc ctc tgc gaa ggg ccc tat gac Phe Val Ala Asp Glu Glu Cys Arg Ala Leu Cys Glu Gly Pro Tyr Asp 

tac gac ggc tac aac tac cta gac tac agc gct gac ctc ttc cag gcc 818

Tyr Asp Gly Tyr Asn Tyr Leu Asp Tyr Ser Ala Asp Leu Phe Gln Ala

255 260 265

atc aca gat cat tac gtc cag gtc ctc aac tgt aag cag aac tgt gtc 866

Ile Thr Asp His Tyr Val Gln Val Leu Asn Cys Lys Gln Asn Cys Val

270 285

acg gag ctg gct tcc cac cca agt agg gaa aag ccc ttt gaa gac ttc 914

Thr Glu Leu Ala Ser His Pro Ser Arg Glu Lys Pro Phe Glu Asp Phe
290 295 300

ctc cct tca cac tat aat tac cta cag ttt gcc tac tac aac att ggg 962

Leu Pro Ser His Tyr Asn Tyr Leu Gln Phe Ala Tyr Tyr Asn Ile Gly

305 310 315

aac tat aca caa get att gaa tgt gee aag ace tae ete ete tte ttt 1010
Asn Tyr Thr Gln Ala Ile Glu Cys Ala Lys Thr Tyr Leu Leu Phe Phe
320 325 330

ccc aat gat gag gtg atg cac cag aat ctg gct tat tac aca gcc atg 1058

Pro Asn Asp Glu Val Met His Gln Asn Leu Ala Tyr Tyr Thr Ala Met

335 340 345

ctt gga gaa gaa gag gcc agc tcc atc agc ccc agg gag aat gcc gag 1106 Leu Gly Glu Glu Glu Ala Ser Ser Ile Ser Pro Arg Glu Asn Ala Glu

the first stands were found the second the first water that the first than the fi

											-					
gaa	tac	cga	cgt	cca	aac	ctg	ttg	gag	aaa	gaa	ctg	ctt	ttc	ttc	gct	1154
Glu	Tyr	Arg	Arg	Pro	Asn	Leu	Leu	Glu	Lys	Glu	Leu	Leu	Phe	Phe	Ala	
				370					375					380		
tat	ma o	att	+++	aas	att	000	+++	ata	ast	000	ant.	tan	taa	not.	000	1202
									gat							1202
Tyr	Asp	lle	Phe	Gly	lle	Pro	Phe	Val	Asp	Pro	Asp	Ser	Trp	Thr	Pro	
			385					390					395			
gaa	gaa	gtg	att	ccc	aag	aga	ttg	caa	gag	aaa	cag	aag	tct	gaa	cgg	1250
Glu	Glu	Val	Ile	Pro	Lys	Arg	Leu	Gln	Glu	Lys	Gln	Lys	Ser	Glu	Arg	
		400					405					410				
		100					100					110				
gaa	aca	gcc	gta	cgc	atc	tcc	cag	gag	att	ggg	aac	ctt	atg	aag	gaa	1298
Glu	Thr	Ala	Val	Arg	Ile	Ser	Gln	Glu	Ile	Gly	Asn	Leu	Met	Lys	G1u	
	415					420					425					
atc	gag	acc	ctt	gtg	gaa	gag	aag	acc	aag	gag	tct	ctg	gat	gtg	agc	1346
									Lys							
							_,_		2,0		501	Dou	пор	, 41		
430					435					440					445	
aga	ctg	acc	cgg	gaa	ggt	ggt	ccc	ctg	ctg	tat	gaa	ggc	atc	agt	ctc	1394
Arg	Leu	Thr	Arg	G1u	Gly	Gly	Pro	Leu	Leu	Tyr	Glu	Gly	Ile	Ser	Leu	
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acc atg aac tcc aaa gtc ttg aat ggc tcc cag cgg gtg gtg atg gat 1442

Thr Met Asn Ser Lys Val Leu Asn Gly Ser Gln Arg Val Val Met Asp
465 470 475

ggt gtg atc tct gat gat gag tgc cag gag ctg cag aga ctg acc aat 1490
Gly Val Ile Ser Asp Asp Glu Cys Gln Glu Leu Gln Arg Leu Thr Asn
480
485
490

gcg gca gca act tcg gga gat ggc tac cga ggt cag acc tcc cca cac 1538

Ala Ala Ala Thr Ser Gly Asp Gly Tyr Arg Gly Gln Thr Ser Pro His

495 500 505

acc cca aat gaa aag ttc tat ggt gtt act gtc ctc aaa gct ctc aag 1586

Thr Pro Asn Glu Lys Phe Tyr Gly Val Thr Val Leu Lys Ala Leu Lys

510 525

ctc ggg cag gaa gga aaa gtt cct ctg cag agt gcc cgc acc gca ctg 1634 Leu Gly Gln Glu Gly Lys Val Pro Leu Gln Ser Ala Arg Thr Ala Leu 530 535 540

caa tagaagagte acaggetgag aggaaggaca gtageeacce egteeacgtg 1687 Gln

gataactgca teetgaatge egaageette atgtgtatea aggageeece agcatacaeg 1747

ttccgggaat acagcgccat cctttacctc aatggcgact tcgatggagg aaacttttac 1807

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<211> 542

<212> PRT

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Met Ala Val Thr Lys Gly Gly Cys Trp His Asp Ala Ser Gly Arg Arg

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Ala Ala Pro Asp Leu Leu Tyr Ala Glu Gly Thr Ala Ala Tyr Ser Arg

35 40 45

Arg Asp Trp Pro Gly Val Val Leu Asn Met Glu Arg Ala Leu Arg Ser
50 55 60

Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Arg Cys Ala
65 70 75 80

Thr Glu Leu Pro Trp Ala Pro Asp Leu Asp Leu Gly Pro Asp Pro Ser

85 90 95

Leu Ser Gln Asp Pro Gly Ala Ala Ala Leu His Asp Leu Arg Phe Phe
100 105 110

Gly Ala Val Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys Leu Gly Pro 115 120 125

Pro Ser Ala His Leu Leu Ser Glu Glu Leu Asp Leu Glu Phe Asn Lys
130 135 140

Arg Ser Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys Ile Asn Lys

145 150 155 160

Leu Glu Lys Ala Val Ala Ala Ala His Thr Phe Phe Val Gly Asn Pro

165 170 175

Glu His Met Glu Met Arg Gln Asn Leu Asp Tyr Tyr Gln Thr Met Ser 180 185 190

Gly Val Lys Glu Ala Asp Phe Arg Asp Leu Glu Ala Lys Pro His Met

195 200 205

His Glu Phe Arg Leu Gly Val Arg Leu Tyr Ser Glu Glu Lys Pro Gln 210 215 220

Glu Ala Val Pro His Leu Glu Ala Ala Leu Gln Glu Tyr Phe Val Ala 225 230 235 240

Asp Glu Glu Cys Arg Ala Leu Cys Glu Gly Pro Tyr Asp Tyr Asp Gly
245 250 255

Tyr Asn Tyr Leu Asp Tyr Ser Ala Asp Leu Phe Gln Ala Ile Thr Asp
260 265 270

His Tyr Val Gln Val Leu Asn Cys Lys Gln Asn Cys Val Thr Glu Leu

											-				
Ala	Ser	His	Pro	Ser	Arg	Glu	Lys	Pro	Phe	G1u	Asp	Phe	Leu	Pro	Ser
	290					295					300				
His	Tyr	Asn	Tyr	Leu	Gln	Phe	Ala	Tyr	Tyr	Asn	Ile	Gly	Asn	Tyr	Thr
305					310					315					320
Gln	Ala	Ile	Glu	Cys	Ala	Lys	Thr	Tyr	Leu	Leu	Phe	Phe	Pro	Asn	Asp
				325					330					335	
Glu	Val	Met	His	Gln	Asn	Leu	Ala	Tyr	Tyr	Thr	Ala	Met	Leu	Gly	Glu
			340					345					350		
Glu	Glu	Ala	Ser	Ser	Ile	Ser	Pro	Arg	G1u	Asn	Ala	Glu	Glu	Tvr	Arg
		355					360	. 0				365		- , -	
											~	500			
Arg	Pro	Asn	Len	Len	Glu	I.vs	Glii	I.e.ii	Len	Phe	Phe	Δ1a	Tyr	Acn	He
3	070				J	_,_	314	204	204		1 110	1114	1 7 1	uch	116

.e 

Phe Gly Ile Pro Phe Val Asp Pro Asp Ser Trp Thr Pro Glu Glu Val 

Ile Pro Lys Arg Leu Gln Glu Lys Gln Lys Ser Glu Arg Glu Thr Ala 

Val Arg Ile Ser Gln Glu Ile Gly Asn Leu Met Lys Glu Ile Glu Thr
420 425 430

Leu Val Glu Glu Lys Thr Lys Glu Ser Leu Asp Val Ser Arg Leu Thr
435 440 445

Arg Glu Gly Gly Pro Leu Leu Tyr Glu Gly Ile Ser Leu Thr Met Asn 450 455 460

Ser Lys Val Leu Asn Gly Ser Gln Arg Val Val Met Asp Gly Val Ile 465 470 475 480

Ser Asp Asp Glu Cys Gln Glu Leu Gln Arg Leu Thr Asn Ala Ala Ala 485 490 495

Thr Ser Gly Asp Gly Tyr Arg Gly Gln Thr Ser Pro His Thr Pro Asn
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Glu Lys Phe Tyr Gly Val Thr Val Leu Lys Ala Leu Lys Leu Gly Gln
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Glu Gly Lys Val Pro Leu Gln Ser Ala Arg Thr Ala Leu Gln
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⟨400⟩ 15

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